

REMARKS

Reconsideration of the above-identified application is requested in view of the foregoing amendment and the following remarks. A separate petition for a two-month extension of time accompanies this paper.

I. Interview Summary

Applicants thank Examiners Dang and Bunner for granting Applicants an in-person interview on June 19, 2007. Compliant with M.P.E.P. § 713.04, Applicants provide this summary of the interview. The § 112 and prior art rejections set forth in the March 2, 2007 Office action were discussed, and claim language to address in particular the § 112 rejections was discussed. The cited patents, 6,060,450 and 6,372,206, were also discussed.

II. Amendments

The Specification has been amended to disclaim the priority benefit of certain applications. In particular, because the pending claims were denied priority to U.S. Provisional Application 60/219,128, U.S. Application Serial No. 09/910,406, and Japanese Application JP 317160. Accordingly, Applicants hereby withdraw the claim of priority to each of these documents. The application continues to claim priority to U.S. Provisional Application 60/552,279, which fully supports the scope of the pending claims.

Claim 1 as amended is directed a method of "decreasing IFN- γ blood levels", as supported, for example, in paragraph [0073]. Claim 1 is also amended to recite "an interferon-tau (IFN τ) having greater than about 80% homology to ovine interferon-tau." Support for the added language can be found, for example, at paragraphs [0038] and [0039]. Applicants note the definition of "ovine IFN τ " is set forth in paragraph [0039].

Claim 1 is also amended to recite that the orally administered dose is between about 6×10^8 – 5×10^{12} , as set forth at paragraph [0126].

Claim 1 is also amended to relate to a therapeutic agent "for treating multiple sclerosis". Agents for treating multiple sclerosis are set forth, for example, in paragraph [0131].

Claim 3 is amended to depend from claim 1, in light of the cancellation of claim 2.

Claim 4 is amended to recite that the elevated IFN- γ level is due to administration of interferon-beta. Support for the amendment can be found, for example, at paragraph [0017].

Claims 2 and 5-11 are canceled, without prejudice or disclaimer.

No new matter has been added by the foregoing amendments.

III. Information Disclosure Statement

The IDS filed on April 26, 2006 allegedly failed to comply with the provisions of 37 C.F.R. § 1.97, 1.98, and M.P.E.P. § 609 with respect to the "R22" [*sic*, "H22"] reference.

The H22 reference is a Statutory Invention Disclosure based on Application Serial No. 06/663,672 and is believed to have been properly cited on the 1449 form. Nonetheless, Applicants provide herewith (i) a copy of the H22 reference, (ii) a copy of the relevant Application Data page from USPTO PAIR, and (iii) a 1449 form citing the H22 reference as it appears in PAIR (i.e., Patent No. H000,022).

Because the IDS originally filed correctly cited the H22 reference, and because the originally-filed IDS was timely filed, Applicants do not believe a fee is due for consideration of the H22 reference. However, the accompanying transmittal form authorizes charging the Representative's Deposit Account should a fee be required for consideration of the document.

IV. Objection to the Specification

The Specification was objected to for failing to identify the current status of the parent applications. As noted above, the priority claims have been amended. This amendment should render the objection moot and withdrawal is requested.

V. Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not sufficiently described in the specification to convey to one skilled in the art that Applicants had possession of the invention at the time of filing the application. In particular, the Examiner asserts that the claims are genus claims, and the specification does not indicate what distinguishing characteristics would be shared by members of the genus.

Claim 1 is amended to focus on a method of decreasing IFN- γ blood level in a *multiple sclerosis* patient being treated with a *multiple sclerosis therapeutic agent*, by administering *ovine* interferon-tau.

For the sake of completeness, the particular phrases the Examiner noted as lacking sufficient descriptive information in the specification, and Applicants' response, are set forth individually below.

"*Interferon-tau*": Claim 1 has been amended to recite "an interferon-tau having greater than about 80% homology to *ovine* interferon-tau". Applicants note the specific definition of "ovine IFN τ " that is provided in paragraph [0039], and refers to SEQ ID NO 2.

"*subject's IFN- γ blood level relative to the IFN- γ blood level in the absence of interferon-tau*": Claim 1 is directed to a method of decreasing the IFN- γ blood level in multiple sclerosis patients being treated with a therapeutic agent used in the treatment of multiple sclerosis, by administering IFN τ . In order for a skilled artisan to understand the metes and bounds of the claim, there must be a way to know whether the IFN- γ blood level decreases due to administration of IFN τ . The phrase being objected to provides a skilled artisan with a means to objectively determine the metes and bounds of the claim, by requiring that the subject's IFN- γ level after treatment with IFN τ be decreased relative to the IFN- γ level in the absence of IFN τ , e.g., before treatment or between IFN τ treatments. The application as originally filed fully supports this concept, for example, in paragraphs [0064], and in the data discussed in paragraphs [0065]-[0067]. In view of the teaching of the specification and the level of knowledge in the art, Applicants submit that there is adequate written description for this phrase in claim 1. Withdrawal of the rejection is respectfully requested.

"therapeutic agent": As amended, this phrase in the claims is specified to be a "therapeutic agent for treating multiple sclerosis." Therapeutic agents for treating multiple sclerosis are set forth in the specification in paragraph [0131]. In view of this amendment, and the support of agents for treating multiple sclerosis, withdrawal is requested.

"disease condition": As amended, the claims no longer recite the phrase "a disease condition". Accordingly, withdrawal of the rejection is respectfully requested.

"autoimmune condition": As amended, the claims no longer recite the term "autoimmune condition." Accordingly, withdrawal of the rejection is respectfully requested.

"subject's symptoms": As amended, the claims no longer recite the term "subject's symptoms." Accordingly, withdrawal of the rejection is respectfully requested.

VI. Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method for treating a patients with multiple sclerosis by reducing the blood level of IFN- γ by administering the IFN- τ protein sequence of SEQ ID NOs: 2 and 3, allegedly does not reasonably provide enablement for a method of preventing an increase in the blood level of IFN- γ in a subject at risk of an elevated IFN- γ blood level dues to (i) administration of a therapeutic agent or (ii) a disease condition. Applicants respectfully traverse the rejection in view of the claim amendments.

The claims as amended are drawn to a method of decreasing IFN- γ blood level in a subject with an elevated IFN- γ blood level due to administration of "a therapeutic agent for treating multiple sclerosis." Therapeutic agents for treating multiple sclerosis are known in the art and described in the specification in paragraph [0131].

The claims are also amended to recite administration of *ovine* interferon-tau, and proteins that are at least about 80% homologous to ovine interferon-tau.

In view of the amendments, Applicants request withdrawal of the rejection.

VII. Rejections Under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claims 1-6 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite with respect to certain terms. The terms objected to by the Examiner, and Applicants' response, are set forth below.

"preventing an increase in blood levels of IFN-γ" Claim 1 as amended no longer recites this phrase, which presumably obviates the rejection.

"subject at risk": Claim 1 as amended no longer recites this phrase, which presumably obviates the rejection.

"therapeutic agent": Claim 1 has been amended to recite a "therapeutic agent for treating multiple sclerosis." Therapeutic agents for treating multiple sclerosis are known in the art and described in the specification in paragraph [0131]. In view of the amendment, the teaching of the specification, and the knowledge of the skilled artisan, Applicants submit that the claim language adequately sets forth the subject matter Applicants regard as their invention, and particularly points out and distinctly defines the metes and bounds of the claimed subject matter.

"disease condition": Claim 1 as amended no longer recites this phrase, which presumably obviates the rejection.

"subject's symptoms": Claim 1 as amended no longer recites this phrase, which presumably obviates the rejection.

In view of the amendments, Applicants request withdrawal of the rejection.

VIII. Obviousness-Type Double Patenting Rejections

Claims 1-6 were provisionally rejected on the ground of non-statutory, obviousness-type double-patenting over claims of 12 related co-pending applications and 2 related issued patents.

The rejections are addressed, in part, by the filing of a Terminal Disclaimer and, in part, by the following arguments.

A. Terminal Disclaimer

The Examiner noted that a timely filed Terminal Disclaimer in compliance with 36 C.F.R. §1.321(c) would overcome an actual or provisional rejection on this ground.

Enclosed herewith is an executed Terminal Disclaimer filed in accordance with C.F.R. §1.321(b) and (c) which disclaims the terminal portion of any patent issuing on the instant application that extends beyond the expiration of U.S. Patent No. 7,083,782 and beyond the expiration of any patents that issue from application nos. 10/592,162; 10/825,068; 10/825,382; 10/884,741; 10/991,653; 11/040,706; 11/078,608; 11/112,369; 11/298,955; 11/298,972; and 11/410,438.

The applicants submit that Terminal Disclaimer overcomes the rejection for obviousness-type double patenting with respect to these documents, and withdrawal of the rejection with respect to these documents is respectfully requested.

B. Analysis of Rejection Based on Application No. 10/346,269 and U.S. Patent No. 7,105,154

Claims 1-6 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-31, 33-34, and 36-37 of application serial no. 10/346,269 and over claims 1-4 of U.S. Patent No. 7,105,154. The rejection is traversed for the following reasons.

A. The Present Claims

Claim 1 as amended is drawn to a method of decreasing IFN- γ blood levels in a subject-with an elevated IFN- γ blood level due to administration of a therapeutic agent for treating multiple sclerosis, comprising orally administering an interferon-tau (IFN τ) having greater than about 80% homology to ovine interferon-tau at a dosage of between about 6×10^8 – 5×10^{12} Units/day, thereby decreasing IFN- γ blood levels compared to those in a subject not administered IFN τ .

B. Analysis

In determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define merely an invention that is merely an obvious variation of an invention claimed in the patent? M.P.E.P. § 804 II.B.1.

B1. The '269 Application

The '269 pending claims are to a method of administering IFN τ comprising orally administering IFN- τ to a person in a fasted state, where the IFN τ achieves an increase in the blood enzyme 2,5-oligoadenylate synthetase (OAS).

OAS is a blood enzyme associated with interferon-alpha regulated antiviral response. The presence of OAS in the blood is suggestive of an antiviral response being mounted by the body.

Instant claims are to a method of reducing IFN- γ blood levels in a person being treated with a therapeutic agent for treating multiple sclerosis by orally administering an interferon-tau (IFN τ) having greater than about 80% homology to ovine interferon-tau at a dose of between about $6 \times 10^8 - 5 \times 10^{12}$ U/day.

Starting from the claims in the '269 application, to arrive at the present claims a skilled artisan must (i) identify the recited dose; and (ii) recognize that the claimed dose will reduce the IFN- γ blood level (iii) in a patient being treated with an MS drug. The '269 claims give no guidance to the claimed dose of between about $6 \times 10^8 - 5 \times 10^{12}$ U/day. Nor do the '269 claims suggest that this dose will reduce IFN- γ blood levels. Nor do the '269 claims suggest that this dose of IFN τ can be orally administered to a patient being treated with a therapeutic agent for multiple sclerosis to achieve a reduction in IFN- γ blood level. Accordingly, Applicants submit that the instant claims are not merely an obvious variation of the claims pending in the '269 application, and withdrawal of the rejection is respectfully requested.

B2. The '154 Patent

The '154 patent claims are to a method of treating, inter alia, an autoimmune condition, comprising oral administration of IFN τ at a dose of at least about 4.9×10^8 U/day to increase OAS, as evidenced by monitoring OAS blood level, and continuing to administer IFN τ .

Starting from the '154 patent claims, to arrive at the present claims one must (i) recognize that the recited dose reduces IFN- γ blood levels (ii) in a patient being treated with an MS drug, and (iii) disregard the '154 claim requirement that the blood OAS level be monitored. Nothing in the '154 patent claims provides guidance on any of (i)-(iii). Accordingly, Applicants submit that the instant claims are not merely an obvious variation of the claims in the '154 patent, and withdrawal of the rejection is respectfully requested.

IX. Rejection Under 35 U.S.C. § 102

Claims 1-2 and 4-6 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Soos et al., U.S. Patent No. 6,060,450 (hereinafter "Soos '450").

Claims 1-3 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Soos et al., U. S. Patent No. 6,372,206 (hereinafter "Soos '206").

The rejection is traversed in view of the foregoing amendments and following remarks.

A. The Pending Claims

Claim 1 is summarized above.

B. The Cited References

Soos '206 discloses oral administration of IFN- τ at a dose range of between about 1×10^5 and 1×10^8 units per day (Col. 4, lines 32-36; Col. 15, lines 47-61).

Soos '450 teaches a method of treating an autoimmune disease, such as multiple sclerosis, by administering interferon-tau. Soos '450 teaches an interferon-tau dose of " 5×10^4 – 20×10^6 to about 500×10^6 units/day or more" (Col. 14, lines 25-27),

and that the interferon-tau can be administered by injection or orally (Col. 15, lines 10-28).

C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. M.P.E.P. § 2131.

C1. Analysis of Soo '206

Soos '206 does not anticipate, expressly or inherently, the present claims because it does not teach (i) a method for decreasing IFN- γ blood levels, (ii) a method for decreasing IFN- γ blood levels in a patient taking a therapeutic agent for multiple sclerosis, or (iii) administering IFN τ at a dose of between about $6 \times 10^8 - 5 \times 10^{12}$ U/day. As noted above, Soos '206 teaches administration of IFN τ at a dose of " $1 \times 10^5 - 1 \times 10^8$ U/day" (Col. 4, lines 32-36). Thus, there is no novelty-destroying teaching in Soos '206 and withdrawal of the rejection is respectfully requested.

C2. Analysis of Soo '450

According to the M.P.E.P. § 2131.03:

When the prior art discloses a range which touches or overlaps with the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with sufficient specificity to constitute an anticipation under the statute.

M.P.E.P. § 2131.03 continues:

What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, and the reference teaches a broad range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims."

The M.P.E.P. illustrates this standard by reference to *Atrofina v. Great Lakes Chem. Corp.* (441 F.3d 991, 78 USPQ2d 1417 (Fed. Cir. 2006)). In *Atrofina*, a prior art temperature range of 100-500 degrees C did not describe with sufficient specificity to be anticipatory the claimed range of 330-450 degrees C (M.P.E.P. § 2131.03II). Additionally, in the *Atrofina* case, even though the prior art preferred range of 150-350 degrees C overlapped with the claimed range (330-450 degrees C), that overlap was insufficient for anticipation.

To apply the M.P.E.P standard to the disclosure of Soos '450, consideration is first given to the teaching of Soos '450. Soos '450 teaches an IFN τ dose range of " $5 \times 10^4 - 20 \times 10^6$ to about 500×10^6 units/day or more" (Col. 14, lines 25-27). Soos '450 teaches that the IFN τ can be administered by injection or orally. The working examples in Soos '450, Examples 1-5, provide a dose of 10^5 U/day of IFN- τ via intraperitoneal injection to mice.

Applying the M.P.E.P standard to the disclosure of Soos '450, it is seen that the dose range of " $5 \times 10^4 - 20 \times 10^6$ to about 500×10^6 units/day or more" taught by Soos '450 is large, encompassing from 5×10^4 to infinity. The claimed range of $6 \times 10^8 - 5 \times 10^{12}$ U/day is a considerably more narrow range. There is nothing in the Soos '450 teaching that would guide a skilled artisan to the more narrow claimed range. Moreover, based on the working examples in Soos '450, a skilled artisan would be led to a dose on the order of 10^5 U/day, which is orders of magnitude lower than the claimed dose range, and led to *injection* of the dose, rather than oral administration of the dose.

Accordingly, Applicants submit that the Soos '450 disclosure of a dose of "... 500×10^6 units/day or more" does not describe with sufficient specificity the claimed range, particularly in view of the working examples in Soos '450 which describe injection of IFN τ in the range of 10^5 Units/day. That is, a skilled artisan, upon reading the disclosure of Soos '450 would be unable to "clearly envisage" the claimed range, as required by M.P.E.P. § 2131.03II.

As evidence that the claimed range of $6 \times 10^8 - 5 \times 10^{12}$ U/day is particularly beneficial in decreasing a subject's IFN- γ blood level suffering from multiple sclerosis, Applicants submit herewith by way of a Declaration of Dr. Chih-Ping Liu ("the Liu Declaration") data from a Phase I Clinical Trial conducted on multiple sclerosis patients. The multiple sclerosis patients were treated for six months with a oral daily dose of IFN- τ of about $9 \times 10^8 - 1.2 \times 10^9$ Units (§9 of the Liu Declaration). Blood samples were taken and MRI scans were done for three months prior to treatment and for six months after treatment (§§7, 8, 10 of the Liu Declaration). During the first three months of treatment, the average serum IFN- γ concentrations decreased from 4.31 pg/mL to 3.93 pg/mL (§13 of the Liu Declaration).

These data establish that IFN- τ when administered orally at a dose in the range of $6 \times 10^8 - 5 \times 10^{12}$ U/day decreases or maintains serum IFN- γ concentrations in human multiple sclerosis patients. The data also shows that IFN- τ when administered orally at a dose in the range of $6 \times 10^8 - 5 \times 10^{12}$ U/day provides a therapeutic benefit to the patients, as evidenced by a reduction in new brain lesions. Notably, lower doses of IFN- τ do not necessarily provide a decrease in serum IFN- γ concentration, as seen in the data set forth in Figs. 2A-2D of the application as filed, where multiple sclerosis patients received an oral IFN- τ dose of 2×10^7 U/day, 6×10^7 U/day, or 1.8×10^8 U/day (page 14, Table 1 of applicant's specification).

Therefore, since all doses of IFN- τ do not necessarily decrease serum IFN- γ concentrations, it cannot be said that oral administration of IFN- τ "inherently" modulates blood cytokine concentrations. Accordingly, Soos '450 does not inherently anticipate the present claims. Moreover, for the reasons given above, Soos '450 does not expressly anticipate the present claims, since Soos '450 does not teach the criticality of the claimed dosage range. Withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.


X. Conclusion

Applicants believe that the present claims comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4328.

Respectfully submitted,
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